Localization of the human TAX-1 gene to 1q32.1: a region implicated in microcephaly and Van der Woude syndrome

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Localization of the human TAX-1 gene to 1q32.1: a region implicated in microcephaly and Van der Woude syndrome

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Cell adhesion molecules TAX-1 (1), TAG-1 (2) and axonin-1 (3) are homologous cell surface glycoproteins expressed in the neural tissue of human, rat and chicken respectively. They are members of a family of proteins composed of repeated immunoglobulin-like (IgC2) and fibronectin type III-like (FNIII) domains that mediate adhesion between components of the nervous system (4). Studies of neurite outgrowth on immobilized axonin-1 indicate that it participates in a heterophilic interaction with L1, a related member of the immunoglobulin superfamily that is expressed on the axons of migrating neurones (5). Recently, we demonstrated that mutations in the human L1 gene give rise to X-linked hydrocephalus, a congenital disorder of brain development (6, 7). In view of the structural similarity and functional association between L1 and TAX-1 homologues we anticipate that disruption of TAX-1 would also result in developmental impairment. As a first step towards determining whether TAX-1 is associated with a genetically mapped inherited disorder we have established its chromosomal location.

Oligonucleotide primers specific for TAX-1 (EMBL accession no. X68274) were used in polymerase chain reactions (PCRs) to amplify a 255 bp product from human DNA. Primers that flank the stop codon (cactccgtggcgatgctgatcctc, forward and atccttgcgtgggtt-ctatcctgcg, reverse) were chosen in order to avoid introns. PCRs using DNA from a panel of somatic cell hybrids indicated that the TAX-1 locus resides on chromosome 1 (Figure 1). Confirmation and refinement of this localization was obtained by fluorescent *in situ* hybridization of a 4.5 kb TAX-1 cDNA clone to metaphase chromosomes. A single band of fluorescence was seen in all cells in the proximal section of 1q32 (1q32.1, Figure 2).

A literature search revealed that the gene for human myosin-binding protein H (MyBP-H), another member of the IgC2/FNIII repeat family, resides within 1q32.1. More interesting, however, is the association of two morphogenetic abnormalities with this region. Van der Woude syndrome, a defect of craniofacial development thought to result from aberrant neural crest cell migration, is genetically linked to 1q32.1 (8) and studies of deletion and translocation events indicate that a gene for microcephaly with mental retardation also resides in this region (9, 10). In view of its potential role in cell migration analysis of the TAX-1 gene in these cases is warranted.

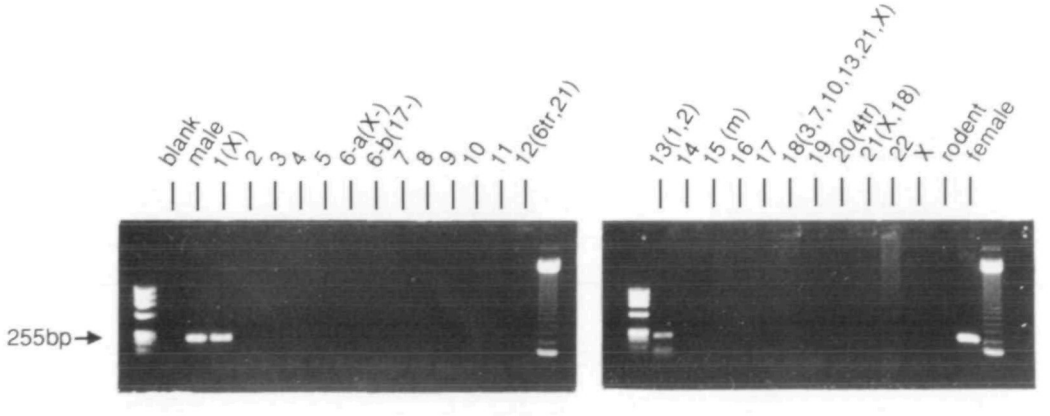

Figure 1. PCR amplification of 255 bp of the TAX-1 locus from genomic DNA. PCRs utilized 10 ng of DNA, and 2 pmols of each primer in 10 μl commercial buffer (Promega) with annealing at 65°C. Human lanes are labelled male and female. Rodent is a mixture of mouse and hamster. The components of hybrids are shown above each lane, the primary mapping chromosome followed by additional components in parentheses. '–' indicates an incomplete chromosome, 'tr' trace quantities and 'm' a marker chromosome. 6-a plus 6-b represents an entire 6. Full details of the hybrids can be obtained from L.R. Molecular weight markers are Hae III-digested φX174 and a 123 bp ladder.

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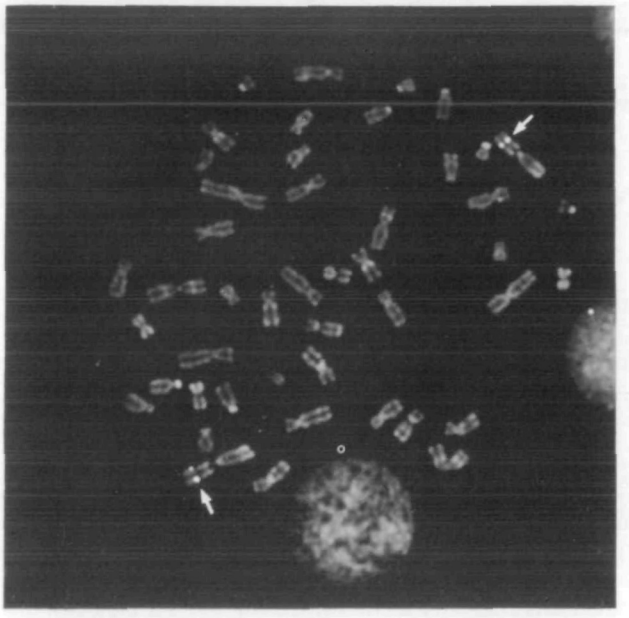

Figure 2. Fluoreacent hybridization of TAX-1 cDNA to metaphase chromosomes from a male lymphoblastoid cell line using the method of Fan *et al.* (11).

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